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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,256	07/23/2004	Takehiko Kitamori	2004_1163A	3964

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EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/502,256	KITAMORI ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *23 July 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement filed 23 July 2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The 5-240872 document has not been provided. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. In claim 1, line 2, the phrase "disposed successively as a micro channel communicating with each other" is vague and indefinite. It is unclear whether the leading-in flow passage part, reaction flow passage part, and detection flow passage

part are each considered a micro channel, or whether the micro channel is the combination of the three parts. The first part of the phrase "disposed successively as a micro channel" seems to indicate that the micro channel is a combination of the three parts, but the second part of the phrase "communicating with each other" implies the opposite, wherein each of the three parts is a micro channel. Applicant is invited to clarify and/or correct the instant phrase to make it less vague and indefinite.

5. In claim 1, line 4, the phrase "bead-bodies supporting antibodies" is vague and indefinite. The specification does not define the phrase and it is unclear what the term "supporting" means and how it limits the instant phrase.

6. In claim 1, lines 4-5, and claim 2, lines 2-3, the term "the bead body" is vague and indefinite. Since the claim 1 recites a plurality of "bead-bodies" (line 4), it is unclear which of the bead-bodies the instant term refers to.

7. In claim 2, line 3, the phrase "flow stopping part of the bead-body" is vague and confusing. The instant claim recites that the "width or the depth of the reaction flow passage part" (lines 2-3) provides stoppage of the flow of bead-bodies. Since it seems that the flow of bead-bodies is stopped by an embodiment separate from the bead-bodies, it is unclear how the flow stopping part of the instant phrase can be at part of the bead-body.

8. In claim 2, line 3, the term "the antibody" is vague and indefinite. Since claim 1 recites a plurality of "antibodies" (line 4), it is unclear which of the antibodies the instant term refers to.

9. In claim 3, line 3, and claim 7, lines 2-3, the term "a detection flow passage part" is vague and indefinite. It is unclear whether the instant term is the same as the detection flow passage part of claim 1 (line 2). In addition, it is unclear whether the plurality of reaction flow passage part micro channels (line 2) each connect to different detection flow passage part micro channels, or connect to the same detection flow passage part micro channel.

10. In claim 5, line 2, the phrase "without contact" is vague and indefinite. The specification does not define the phrase and it is unclear what embodiment is not contacted.

11. Claim 1 recites the limitation "the reaction flow passage part micro channel" in lines 3-4. There is insufficient antecedent basis for this limitation in the claim.

12. Claim 2 recites the limitation "the flow stopping part of the bead-body" in line 3. There is insufficient antecedent basis for this limitation in the claim.

13. Claim 3 recites the limitations "the front side" in line 3 and "the detection point" in lines 3-4. There is insufficient antecedent basis for these limitations in the claim.

14. Claim 4 recites the limitations "the antigen antibody reaction with the enzyme" in lines 2-3, and "the label" in line 3. There is insufficient antecedent basis for these limitations in the claim.

15. Claim 7 recites the limitations "the front side" and "the detection point" in line 3. There is insufficient antecedent basis for these limitations in the claim.

16. Claims 8-10 recite the limitations "the antigen antibody reaction with the enzyme" in line 2, and "the label" in line 3. There is insufficient antecedent basis for these limitations in the claim.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

18. Claims 1-2 are rejected under 35 U.S.C. 102(e) as being anticipated by Harrison et al (US 6,432,290 B1).

Harrison et al teach a microfluidic chip comprising a chamber 4 (i.e. reaction flow passage part), narrow side channel 5 (i.e. liquid leading-in flow passage part), and main channel 11 with reservoirs 1 and 2 (i.e. detection flow passage), wherein narrow side channel 5 connects to chamber 4 (i.e. inlet part) and weirs 6 and 7 (i.e. flow stopping part) prevent beads from moving into channel 11 since the weirs are not as high as the main channel 11 is deep (i.e. depth of reaction flow passage part sufficiently shallow), only providing flow gaps 14 and 15 that do not allow beads to pass through. See column 5, lines 6-43; column 8, lines 54-61; and Figures 1A-B and 2A, and 3A. In addition, Harrison et al teach that antibodies can be placed on the beads for immunosorbent assays (i.e. bead-bodies supporting antibodies), and that the beads can be used for bead-based immunoassays for enzymes (i.e. enzyme immunoassay). See column 12, lines 35-37 and 57-60.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claims 4-5, 8, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al (US 6,432,290 B1) in view of Eteshola et al (Sensors and Actuators B, 2001).

Harrison et al reference has been disclosed above, and additionally teaches that light generated from an enzyme reaction is detected downstream from the enzyme bed (i.e. enzyme reaction products is tested by the detection flow passage part). See column 13, lines 4-7; and column 13, line 64 to column 14, line 4. However, Harrison et

al fail to teach that the enzyme reaction product is produced by antigen antibody reaction with an enzyme.

Eteshola et al teach the downstream detection of a fluorophore in a microfluidic device, wherein the fluorophore is generated from an HPR-catalyzed fluorogenic substrate conversion, in order to provide a fast, simply, and sensitive immunoassay that does not require a multistate, labor-intensive process with long incubation periods and washes. See page 129, left column, 2nd paragraph to right column, 1st paragraph; and page 130, right column, 3rd paragraph to page 131, left column, 1st paragraph; and Figure 1 and caption.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus and method of Harrison et al with the downstream detection of a fluorophore in a microfluidic device, wherein the fluorophore is generated from an HPR-catalyzed fluorogenic substrate conversion, as taught by Eteshola et al, in order to provide a fast, simply, and sensitive ELISA that does not require a multistate, labor-intensive process with long incubation periods and washes. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the downstream detection of a fluorophore in an ELISA, as taught by Eteshola et al, in the apparatus and method of Harrison et al, since Harrison et al teach a microfluidic device with antigen capture for immunoassays and downstream detection, and the fluorophore production and detection of Eteshola et al is also in a microfluidic device with antigen capture and means for downstream detection.

With regards to claims 5 and 11, since Eteshola et al teach fluorescence detection, the fluorophore is therefore optically detected and does not require physical contact with the detection device.

23. Claims 3 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al (US 6,432,290 B1) in view of Yukiko et al (JP 2000-162184).

Harrison et al reference has been disclosed above, but fails to teach a plurality of reaction flow passage part micro channels disposed side by side that communicate with a detection flow passage part micro channel on the front side with respect to the detection point.

Yukiko et al teach a device with a plurality of channels 12a-d, in order to provide an apparatus in which a plurality of samples can be analyzed at high-throughput for analysis without contamination, thereby providing high sensitivity analysis. See page 7, section 0008; and Figure 1.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Harrison et al with a plurality of channels 12a-d, as taught by Yukiko et al, in order to provide an apparatus in which a plurality of samples can be analyzed at high-throughput for analysis without contamination, thereby providing high sensitivity analysis. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a plurality of channels, as taught by Yukiko et al, in the apparatus of Harrison et al, since Harrison et

al teach a microfluidic device with channels, and the channels of Yukiko et al are integrated into a microfluidic device.

24. Claims 6, 14, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al (US 6,432,290 B1) in view of Eteshola et al (Sensors and Actuators B, 2001) as applied to claims 1, 4-5, and 8 above, and further in view of Sato et al (Analytical Sciences, 1999).

Harrison et al and Eteshola et al references have been disclosed above, but fail to teach that the enzyme reaction product is detected by a thermal lens microscope system.

Sato et al teach a thermal-lens microscope to detect optical irradiation in a microfluidic channel, in order to provide a means of optical detection with ultrahigh sensitivity and stability. See page 526, left column, 1st paragraph to right column, 1st paragraph; and Figure 1 and caption. In addition, Sato et al teach applications of the thermal-lens microscope to enzyme and immunoassays. See page 525, left column, 2nd paragraph,

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Harrison et al and Eteshola et al with a thermal-lens microscope to detect optical irradiation in a microfluidic channel, as taught by Sato et al, in order to provide a means of optical detection with ultrahigh sensitivity and stability. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a thermal lens microscope, as taught by

Sato et al, in the apparatus of Harrison et al and Eteshola et al, since Harrison et al and Eteshola et al teach a detection means to detect enzyme reactions that give off light, and the thermal lens microscope of Sato et al performs detection by through optical irradiation of enzyme reactions.

25. Claims 9-10 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al (US 6,432,290 B1) in view of Yukiko et al (JP 2000-162184) as applied to claims 1, 3 and 7 above, and further in view of Eteshola et al (Sensors and Actuators B, 2001).

Harrison et al and Yukiko et al references have been disclosed above, and Harrison et al additionally teach that light generated from an enzyme reaction is detected downstream from the enzyme bed (i.e. enzyme reaction products is tested by the detection flow passage part). See column 13, lines 4-7; and column 13, line 64 to column 14, line 4. However, Harrison et al and Yukiko et al fail to teach that the enzyme reaction product is produced by antigen antibody reaction with an enzyme.

Eteshola et al teach the downstream detection of a fluorophore in a microfluidic device, wherein the fluorophore is generated from an HPR-catalyzed fluorogenic substrate conversion, in order to provide a fast, simply, and sensitive immunoassay that does not require a multistate, labor-intensive process with long incubation periods and washes. See page 129, left column, 2nd paragraph to right column, 1st paragraph; and page 130, right column, 3rd paragraph to page 131, left column, 1st paragraph; and Figure 1 and caption.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus and method of Harrison et al and Yukiko et al with the downstream detection of a fluorophore in a microfluidic device, wherein the fluorophore is generated from an HPR-catalyzed fluorogenic substrate conversion, as taught by Eteshola et al, in order to provide a fast, simply, and sensitive ELISA that does not require a multistate, labor-intensive process with long incubation periods and washes. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the downstream detection of a fluorophore in an ELISA, as taught by Eteshola et al, in the apparatus and method of Harrison et al and Yukiko et al, since Harrison et al and Yukiko et al teach a microfluidic device with antigen capture for immunoassays and downstream detection, and the fluorophore production and detection of Eteshola et al is also in a microfluidic device with antigen capture and downstream detection.

With regards to claims 12-13, since Eteshola et al teach fluorescence detection, the fluorophore is therefore optically detected and does not require physical contact with the detection device.

26. Claims 15-16 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al (US 6,432,290 B1) in view of Yukiko et al (JP 2000-162184) as applied to claims 1, 3 and 7 above, and further in view of Eteshola et al (Sensors and Actuators B, 2001) as applied to claims 9-10 and 12-13 above, and further in view of Sato et al (Analytical Sciences, 1999).

Harrison et al, Yukiko et al, and Eteshola et al references have been disclosed above, but fail to teach that the enzyme reaction product is detected by a thermal lens microscope system.

Sato et al teach a thermal-lens microscope to detect optical irradiation in a microfluidic channel, in order to provide a means of optical detection with ultrahigh sensitivity and stability. See page 526, left column, 1st paragraph to right column, 1st paragraph; and Figure 1 and caption.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Harrison et al, Yukiko et al, and Eteshola et al with a thermal-lens microscope to detect optical irradiation in a microfluidic channel, as taught by Sato et al, in order to provide a means of optical detection with ultrahigh sensitivity and stability. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a thermal lens microscope, as taught by Sato et al, in the apparatus of Harrison et al, Yukiko et al, and Eteshola et al, since Harrison et al, Yukiko et al, and Eteshola et al teach a detection means to detect enzyme reactions that give off light, and the thermal lens microscope of Sato et al performs detection by through optical irradiation of enzyme reactions.

Conclusion

27. No claims are allowed.

28. The prior art made of record and not relied upon is considered pertinent to Applicants' disclosure:

Hillman et al (US 4,963,498) teach a capillary flow device with antibody-antigen binding and detection.

Wilding et al (US 5,498,392) teach microscale flow devices with biomolecules immobilized on beads.

Tanaka et al (Journal of Chromatography A, 2000) teach a Y-shaped microfluidic channel network for enzyme reactions and detection with a thermal lens microscope.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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05/24/05